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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/528,500
Filing Date: March 18, 2005
Appellant(s): DE MORAES BARROS ET AL.

David Carstens
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 11 November 2009 appealing from the Office action mailed 09 January 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Ropke et al. Topical Application of Pothomorphe unbellata Root Extract Prevents alph-Tocopherol from Depletion after UV-Irradiation on Hairless Mouse Skin. Free Radical Biol. Med. Vol. 33, Issue 2 (July 2002), Abstract #527.

Ropke et al. Evaluation of the Antioxidant Activity of Pothomorphe unbellata L. MIQ on the Skin. Annals of the 14th National Cosmetology Congress of the Brazilian Cosmetology Association. 2000, pp. 483-500. Full English translation thereof (23 pages).

6,165,479 Wheeler 12-2000

JP 2001-122763 Uchiyama et al. 08-2001
Full computer-assisted English translation thereof .

Barros et al. Antioxidant Activity of Ethanolic Extracts of Pothomorphe umbellata L. Miq. (Pariparoba). Vol. 48, No. 1/2 (January/April 1996), pp. 114-116.

Desmarchelier et al. 4-Nerolidylcatechol from Pothomorphe spp. Scavenges Peroxyl Radicals and Inhibits Fe(II)-Dependent DNA Damage. Planta Med. Vol. 63 (1997), pp. 561-563.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

Claims 24, 27, and 28 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 24 and 28 recite various numerical range limitations regarding the amounts of elements a) through c) which are not supported by the instant specification (i.e., the Examiner could not find support for the narrower ranges instantly claimed, nor did Applicants particular point to such support within the instant specification). In other words, the instant specification does not support the following numerical percentage ranges:

- a range from 0.01 to 2.0% of carboxymethylcellulose (i.e., the specification appears to only support a range from 0.01 to 10.0% of this element).
- a range from 5.0 to 20.0% of propylene glycol (i.e., the specification appears to only support a range from 0.001 to 50.0% of this element).
- a range from 0.1 to 1.0% of methylparaben (i.e., the specification appears to only support a range from 0.001 to 3.0% of this element).

Claim Rejections - 35 USC § 103

Claims 24, 27, and 28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ropke et al. (Free Radical Biol. Med., Vol 33, Issue 2, Abstract #527, 15 July 2002) and Ropke et al. (Annals of the 14th National Cosmetology Congress of the Brazilian Cosmetology Assoc, 2000 - including entire English Translation of this document) in view of Wheeler (US 6,165,479) and, if necessary, the admitted state of the art.

The two cited Ropke et al. references each beneficially teach topical gel compositions having strong therapeutic antioxidant activity which comprise an extract of *Pothomorphe umbellata*, whereby the gel compositions comprise 4-nerolidylcatechol (on the basis of the *Pothomorphe umbellata* extract). In addition, the second Ropke et al. reference (2000) discloses a topical compositions presented in a gel form (i.e., within diadermine - an oil/water emulsion) comprising an extract of *Pothomorphe umbellata*, whereby the topical compositions comprises 0.2%, 0.05, 0.1, 0.2, and 2% (p/p) of 4-nerolidylcatechol therein; and further that the dry extract contains 2.35% of 4-nerolidylcatechol therein (see, e.g., page 8 of English translation) - thus, apparently within the instantly claimed ranges therein. The cited Ropke et al. references also teach topically applying the gel compositions to the skin of hairless mice (see Abstract# S527 of first Ropke et al. reference; and entire English translation including pages 2-5, 7-9,13-14, 16, and final paragraph on page 18 of the second Ropke et al. reference) - e.g., as a photoprotective agent for treating skin cancer and/or aging. Neither of the Ropke et al. references expressly teaches providing the skin therapeutic *Pothomorphe umbellata* extract within a skin gel composition containing carboxymethylcellulose, propylene glycol, and methylparaben, as instantly claimed.

Wheeler beneficially teaches that carboxymethylcellulose, propylene glycol, and methylparaben are well known conventional ingredients within skin therapeutic compositions such as skin gels, including those containing an antioxidant therein (see entire reference including col 2, line 58 - col 4, line 67). Further, as readily admitted by Appellants, the instantly claimed dermocosmetic composition can be prepared in accordance with prior art methods for topical use - such as one containing carboxymethylcellulose, propylene glycol, and methylparaben (see, e.g., page 11, lines 1-5).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to incorporate the *Pothomorphe umbellata* extract preparation having strong therapeutic antioxidant activity as taught by each of the Ropke et al. references into a conventional skin therapeutic formulation (e.g., as an effective antioxidant) - including a skin gel, containing the commonly-employed skin care ingredients carboxymethylcellulose, propylene glycol, and methylparaben therein based upon the beneficial teachings provided by Wheeler, as well as (if necessary) the admitted state of the prior art, with respect to their well known conventional use therein, as discussed above. Accordingly, the adjustment of this and other types of conventional working conditions (e.g., determining an appropriate amount range of such conventional ingredients therein) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Thus, the invention as a whole was clearly *prima facie* obvious over the references (and, if necessary, the admitted state of the art) especially in the absence of clear and convincing evidence to the contrary.

Claims 24, 27, and 28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Uchiyama et al. (JP 2001122763 - full computer-assisted English translation enclosed) in view of Barros et al. (Ciencia e Cultura, 1996) and Desmarchelier et al. (Planta Med, 1997), and further in view of Wheeler (US 6,165,479) and, if necessary, the admitted state of the art.

Uchimyama et al. beneficially teach a topical skin composition (e.g., in the form of a lotion, cream, etc.) comprising an extract of *Pothomorphe umbellata*.(including an alcoholic extract such as an ethanolic or methanolic extract - please note, as evidenced by Barros et al. and Desmarchelier et al., such an alcoholic extract would inherently comprise the naturally occurring compound 4-nerolidylcatechol) as an active skin therapeutic ingredient therein (e.g., useful against skin aging caused by ultraviolet rays among other therapeutic effects), as well as topically applying such a composition to the skin. Uchimyama et al. also beneficially teach that the extract composition has antioxidant activity (i.e., oxygen-eliminating ability) - such as instantly disclosed (see entire computer-assisted English translation including paragraphs [0002], [0007] - [0016], [0021], [0028], [0034]-0035], [0037], and Tables).

The Barros et al. and Desmarchelier et al. references each beneficially teach a composition comprising an alcoholic (ethanolic - Barros et al; methanolic - Desmarchelier et al) extract of *Pothomorphe umbellata* - whereby the extracts demonstrate strong antioxidant activity (such as instantly disclosed) which contain the compound 4-nerolidylcatechol - apparently within the instantly claimed percentage range therein (see entire documents including *Abstract* and *Materials and Methods*).

None of the above references, including Uchimyama et al., expressly teach providing the skin therapeutic *Pothomorphe umbellata* extract within a skin gel composition - including one containing carboxymethylcellulose, propylene glycol, and methylparaben, as instantly claimed.

Wheeler beneficially teaches that carboxymethylcellulose, propylene glycol, and methylparaben are well known conventional ingredients within skin therapeutic compositions such as skin gels, including those containing an antioxidant therein (see entire reference including col 2, line 58 - col 4, line 67). Further, as readily admitted by Appellants, the instantly claimed dermocosmetic composition can be prepared in accordance with prior art methods for topical use - such as one containing carboxymethylcellulose, propylene glycol, and methylparaben (see, e.g., page 11, lines 1-5).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to incorporate an alcoholic (e.g., ethanolic or methanolic) extract of *Pothomorphe umbellata* within the skin therapeutic composition (having antioxidant activity) as taught by Uchimyama et al, especially since Uchimyama et al. beneficially teaches that ethanolic and methanolic solvents are effective solvents to employ, and Barros et al. and Desmarchelier et al. beneficially teaches that such alcoholic solvents provide a *Pothomorphe umbellata* extract having strong antioxidant activity (in addition, it should again be noted that, as evidenced by Desmarchelier et al., such an alcoholic extract would inherently comprise the naturally-occurring compound 4-nerolidylcatechol therein). It would further have been obvious to one of ordinary skill in the art at the time the claimed invention was made to incorporate such a *Pothomorphe umbellata* extract into a conventional skin therapeutic formulation (e.g., as an effective antioxidant) - including a skin gel, containing the commonly-employed skin care ingredients

carboxymethylcellulose, propylene glycol, and methylparaben therein based upon the beneficial teachings provided by Wheeler, as well as (if necessary) the admitted state of the prior art, with respect to their well known conventional use therein, as discussed above. Accordingly, the adjustment of this and other types of conventional working conditions (e.g., determining an appropriate amount range of such ingredients therein) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Thus, the invention as a whole was *prima facie* obvious over the references (and, if necessary, the admitted state of the art) especially in the absence of clear and convincing evidence to the contrary.

(10) Response to Argument

With respect to the USC 112, first paragraph rejection, Appellants argue that ranges in a claim can be narrower than those disclosed in specification and that the instantly claimed ranges are within the ranges disclosed in the specification, and point to various legal decisions to support their position. However, in the present case, there is absolutely no teaching within the instant specification regarding the instantly claimed narrower numerical end-point designations of elements (a), (b), and (c). That is, the specification fails to teach one or both of the newly recited end-point numerical percentages for each of elements (a), (b), and (c) with respect to the amended narrower numerical end-point percentage ranges instant claimed (please note that the unsupported numerical end-point for each element is underlined below), as follows:

For element (a), the instant specification fails to teach a range of 0.01 to 2.0% of carboxymethylcellulose within the recited gel composition (i.e., the specification only provides

support for a range of 0.01 to 10.0% carboxymethylcellulose - as originally claimed and as disclosed on page 11, lines 1-13, of the instant specification).

For element (b), the instant specification fails to teach a range of 5.0 to 20.0% of propylene glycol within the recited gel composition (i.e., the specification only provides support for a range of 0.001 to 50.0% propylene glycol - as originally claimed and as disclosed on page 11, lines 1-13, of the instant specification).

For element (c), the instant specification fails to teach a range of 0.1 to 1.0% on methylparaben within the recited gel composition (i.e., the specification only provides support for a range of 0.001 to 3.0% methylparaben - as originally claimed and as disclosed on page 11, lines 1-13, of the instant specification).

It is also noted that within section V (Summary of the Claimed Subject Matter) of the Appeal Brief, it appears to the examiner that Appellants are indicating support for the instantly claimed narrower numerical ranges of elements (a)-(c) can be found on page 11 - lines 7-9, respectively, of the specification. However, please note that the illustrative example composition shown on page 11 (including lines 7-9) of the specification recites the broader numerical ranges for each of elements (a)-(c) therein - as originally claimed.

Appellants further argue that the recited range of element (d) - i.e., 4-nerolidylcatechol within the composition, as claimed in claim 24 and 28 (i.e., 0.005 to 20.0%), is fully supported by the specification. The examiner agrees which is why the examiner did not state that the recited range of 4-nerolidylcatechol within the claimed gel composition was new matter in the USC 112 first paragraph rejection set forth in the previous Office action (and restated above). Please note that the only issues brought up in the USC 112, first paragraph rejection set forth in

the previous Office action (and restated above) concern the instantly claimed new matter recitations of elements (a), (b), and (c) with respect to the recited narrower numerical cut-off ranges thereof, as fully discussed above.

Appellants additionally argue that the specification mentions that a possible source for 4-nerolidylcatechol is a *Pothomorphe umbellata* root extract and that, although not specifically mentioned in the specification, someone skilled in the art would know that 4-nerolidylcatechol could be obtained by any other means. However, it is reemphasized that the only issues brought up in the USC 112, first paragraph rejection set forth in the previous Office action (and restated above) concern the instantly claimed new matter recitations of elements (a), (b), and (c) with respect to the recited narrower numerical cut-off ranges thereof, as fully discussed above.

With respect to the two USC 103 rejections of record, Appellants argue that although the antioxidant activity of *Pariparoba* (also known as *Pothomorphe umbellata*) was known, it is not obvious to imagine which specific gel formulation serves as a vehicle for this drug in order to obtain a therapeutically effective gel composition, that there are not specific studies about the performance of active principle of this plant in the oxidative stress caused by UV radiation, that Figure 3 shows the effectiveness of the proposed vehicle showing that 4-nerolidylcatechol is present on (into) the skin, that in the present application, it was demonstrated for the first time the activity *in vivo* of the extract in mice chronically exposed to UV radiation, and that the present invention is not based on antioxidant activity, but on photoprotective activity (photodamage) - thus it is not possible to say that any substance that presents antioxidant activity is a photoprotector.

However, with respect to the first USC 103 rejection of record, the two primary Ropke et al. references each beneficially teach topical gel compositions having strong therapeutic antioxidant activity which comprise an extract of *Pothomorphe umbellata*, whereby the gel compositions comprise 4-nerolidylcatechol (on the basis of the *Pothomorphe umbellata* extract), including 0.1% 4-nerolidylcatechol (on the basis of the *Pothomorphe umbellata* extract) in the gel composition of the first Ropke et al. reference (2002). In addition, the second Ropke et al. reference (2000) discloses topical compositions presented in a gel form (i.e., within diadermine - an oil/water emulsion) comprising an extract of *Pothomorphe umbellata*, whereby the topical compositions comprise 0.2%, 0.05, 0.1, 0.2, and 2% (p/p) of 4-nerolidylcatechol therein; and further that the dry extract contains 2.35% of 4-nerolidylcatechol therein (see, e.g., page 8 of English translation) - thus, apparently within the instantly claimed ranges therein. The cited Ropke et al. references also teach topically applying the topical and/or gel compositions to the skin of hairless mice - e.g., as a photoprotective agent for treating skin cancer and/or aging (as fully discussed above). With respect to the second USC 103 rejection of record, the primary reference of Uchimyama et al. beneficially teaches a topical skin composition (e.g., in the form of a lotion, cream, etc.) comprising an extract of *Pothomorphe umbellata*.(including an alcoholic extract such as an ethanolic or methanolic extract - please note, as evidenced by Barros et al. and Desmarchelier et al., such an alcoholic extract would inherently comprise the naturally occurring compound 4-nerolidylcatechol as an active skin therapeutic ingredient therein - e.g., useful against skin aging caused by ultraviolet rays among other therapeutic effects (as fully discussed above).

Appellants further argue that it must, in fact, be noted that it is the specific combination of the components of the claimed gel composition that grants its therapeutic properties as it is well known in the art that a given antioxidant must permeate the stratum corneum so that the active principle reaches the viable skin to exert its antioxidant activity, and that this permeation depends not only on the structure of the antioxidant compound itself but also on the specific formulation used and the interaction between the compound itself and the formulation used with the skin, that Example 1 of the specification demonstrates that the claimed composition indeed has the ability to deliver 4-nerolidylcatechol into the skin (FIG 3) and it can therefore be used topically for therapeutic purposes; and also that Examples 1 and 2 specifically demonstrate that a gel containing 0.1% 4-nerolidylcatechol preserves the levels of tocopherol in the skin of irradiated mice thus protecting it against degradation by UV-radiation. In addition, Appellants argue that although the examiner states that Wheeler et al. teaches that carboxymethylcellulose, propylene glycol, and methylparaben are well known conventional ingredients within skin therapeutic compositions, the present invention is not limited to a simple addition of an antioxidant to the composition, but a composition that presents photoprotective activity *in vivo*, wherein lies the non-obviousness of the invention. However, it should be noted that the example illustrated on page 11, lines 1-13, of the instant specification is "the chosen formulation" with respect to a functionally-effective topical dermocosmetic composition, and that this chosen formulation (which can be made by prior art methods) may comprise 0.01 to 10.0% of carboxymethylcellulose, 0.001 to 50% of propylene glycol, and 0.001 to 3.0% of methylparaben, all of which are conventional amount ranges used in the topical cosmetic art, including within therapeutic topical cosmetics containing plant extracts therein (such as beneficially disclosed by

Wheeler who teaches such amount ranges of carboxymethylcellulose, propylene glycol, and methylparaben within a topical composition to which a therapeutic plant extract, including an aqueous or alcoholic plant extract, can be added - see entire Wheeler document including col 2, line 58 - col 4, line 67). Although Appellants have amended the claims so as to narrow the amount ranges for each of these three commonly-employed topical cosmetic ingredients (see USC 112, first paragraph rejection concerning these narrower numerical range limitations) therein, without clear evidence to the contrary, these ranges would not appear to materially alter the skin permeation properties of the instantly claimed gel (and are, thus, still considered obvious in the art of topical dermocosmetics), especially given that "the chosen formulation" illustrated within the instant specification is one which can contain the disclosed broader ranges of carboxymethylcellulose, propylene glycol, and methylparaben therein (and which can admittedly be made by prior art methods) - as per the express teachings of the instant specification (as disclosed on page 11, lines 1-13, therein). In addition, it should be noted that Examples 1 and 2 (on pages 13-16 of the instant specification) do not recite the amount ranges for any of these three common cosmetic ingredients (i.e., carboxymethylcellulose, propylene glycol, and methylparaben) therein. Accordingly, one of ordinary skill in the art would reasonably discern that the composition used within Examples 1 and 2 of the instant specification is referring to the topical dermocosmetic formulation taught on page 11 with respect to a gel composition that effectively functions within the broader ranges of carboxymethylcellulose, propylene glycol, and methylparaben (as recited on page 11 of the illustrated chosen formulation, and as originally claimed) therein - including in terms of one which effectively provides for the argued skin permeation properties with respect to appropriately allowing the permeation of the active

ingredient 4-nerolidylcatechol (contained within the *Pothomorphe umbellata* extracts) into the skin.

Appellants further argue that although the 2002 Ropke reference mentions in the summary the use of a gel, the components of said gel were not specified. However, as stated by Appellants, this summary article does in fact expressly teach a gel composition - i.e., the 2002 Ropke reference beneficially teaches a topical gel composition having strong therapeutic antioxidant activity which comprises an extract of *Pothomorphe umbellata*, whereby the gel composition comprises 0.1% 4-nerolidylcatechol (on the basis of the *Pothomorphe umbellata* extract) - i.e., within the instantly claimed percentage range, therein. Appellants also argue that the 2002 Ropke reference should not be considered prior art by the examiner since it was published by the inventors themselves, two months prior to the filing of the Brazilian priority application which was filed 18 September 2002. However, the 2002 Ropke et al. reference (which was publish July 2002) was published approximately 2 years, 8 months before the U.S. filing date of the present application and (as stated by Appellants) 2 months before the foreign priority date of the cited Brazilian application. Accordingly, the 2002 Ropke reference constitutes prior art of over the instantly claimed invention (since the very earliest date Appellants are entitled to is the foreign priority date of 18 September 2002).

Appellants further argue that the 2000 Ropke reference does not teach a gel composition, but instead diadermine compositions. However, without an express definition within the instant specification defining such a "gel composition", the Examiner maintains that the water/oil emulsion taught by the 2000 Ropke reference reasonably reads upon a "gel composition" as

instantly claimed - whereby the composition comprises an extract of *Pothomorphe umbellata* containing 0.2%, 0.05, 0.1, 0.2, and 2% (p/p) of 4-nerolidylcatechol therein.

Appellants also argue that, according to the Examiner, any antioxidants added to any formulation would produce the effect shown in claim 28. However, the Examiner never argued or made any statements to this effect.

Appellants additionally argue that the examiner says on page 3, paragraph 3, of the previous Office action that "none of the above references, including Uchimyama et al., expressly teach providing the skin therapeutic *Pothomorphe umbellata* extract within a skin gel composition - including one containing carboxymethylcellulose, propylene glycol, and methylparaben, as instantly claimed" which contradicts Examiner's earlier statements. However, this statement was only made in the second USC 103 rejection of record and was referring to the teachings of Uchimyama et al., Barros et al., and Desmarchelier et al., none of which expressly teach providing the skin therapeutic *Pothomorphe umbellata* extract within a skin gel composition - including one containing carboxymethylcellulose, propylene glycol, and methylparaben, as instantly claimed (this statement was not referring to the first USC 103 rejection of record).

Appellants conclude their arguments by stating that based on the cited references, it would not have been obvious to imagine an extract of *Pothomorphe* in a gel formulation with the specified components, and that it would not be possible to foresee that such gel composition with *Pothomorphe umbellata* extract had photoprotective activity. However, for the reasons fully discussed in the previous Office action (and restated above), the examiner disagrees. In addition, Appellants' arguments are not commensurate in scope to the instantly claimed gel composition

which is not limited to one having such photoprotective activity (nor to an extract of *Pothomorphe umbellata*, per se).

With respect to other generalized statements by Appellants regarding the criteria for establishing a *prima facie* case of obviousness, Appellants have argued and discussed the references within each of the two USC 103 rejections individually without clearly addressing the combined teachings used in each rejection. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Appellants' claimed invention fails to patentably distinguish over the state of the art represented by the references.

Accordingly, the examiner contends that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide a topical therapeutic gel composition comprising the recited percentage range of 4-nerolidylcatechol (including on the basis of *Pothomorphe umbellata* extract), in combination with result-effective amounts of carboxymethylcellulose, propylene glycol, and methylparaben therein (as well as to topically apply such a gel composition, including to photodamaged, aged, and/or cancerous/precancerous skin of a subject in need thereof) based upon the beneficial prior art teachings fully discussed above under each USC 103 rejection.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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